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Original Research Article

Palliative intensity modulated radiotherapy of bone metastases based on diagnostic instead of planning computed tomography scans

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ABSTRACT

Background and purpose: Radiotherapy (RT) treatment planning is as a standard based on a computed tomography (CT) scan obtained at the planning stage (pCT), while most of the decisions whether to treat by RT are based on diagnostic CT scans (dCT). Bone metastases (BM) are the most common palliative RT target. The objective of this study was to investigate if a palliative RT treatment plan of BMs could be made based on a dCT with sufficient accuracy and safety, without sacrificing any treatment quality.

Materials and methods: A retrospective study with 60 BMs of 8 anatomical sites was performed. RT planning was performed using intensity-modulated radiation therapy/volumetric modulated arc therapy techniques in dCT and transferred to pCT. The dose of clinical target volumes (CTVs), $D(CTV_{V95\%,\ V50\%})$, were compared between plans for dCT and pCT. Patient setup was investigated in cone-beam CT scans.

Results: The differences of $D(CTV_{V95\%,\ V50\%})$ between dCT and pCT plans were the lowest in the pelvis (1.0%, 1.1%), lumbar spine (0.6%, 0.7%) and thoracic spine (0.7%, 2.1%), while the differences were higher in cervical spine (3.7%, 1.9%), long bones (2.3%, 0.8%), and costae (1.6%, 1.4%). The patient set-up was acceptable for 100% of the pelvic and lumbar, for 92% of thoracic spine cases, and for <80% of cases in other sites.

Conclusion: This study showed the feasibility of using dCT images in palliative RT planning of BMs in thoracic, lumbar spine and pelvic sites, indicating the potential suitability of this strategy for clinical use.

1. Introduction

The number of cancer patients is increasing in the population as a result to better prognosis with longer life expectancy, in addition to overall higher cancer rates. Radiotherapy (RT) is used in cancer treatment in up to 60% of all cancer patients in high-income countries, and the intention is palliative in 40–70% of all RT courses [1].

Bone metastases (BM) are frequent in cancer patients. The incidence of BMs varies substantially by tumor type. Approximately 5–7% of adult solid cancer patients are diagnosed with metastasis to bone over the course of first five years of their disease [2,3]. BMs can cause severe disadvantage, such as intense pain, pathologic fractures, and hypercalcemia, with the most devastating being spinal cord compression requiring immediate action. Palliative RT given to BMs is often highly successful in treating symptoms [4].

Despite the explicit objective to increase patient's quality of life, by alleviating pain and reducing symptoms, the course of palliative RT remains strenuous and time-consuming to the patient. By reducing hospital appointments occurring on several occasions, the RT treatment pathway would be lighter to the patient.

To answer to the increasing need of planning CT (pCT) times and to accelerate the treatment pathway of painful patients requiring treatment, we investigated whether using a diagnostic CT (dCT) to obtain a palliative RT treatment plan could be used. The idea is reasoned, as in referral to the RT unit, dCT images are often available when deciding whether a patient benefits from RT with palliative intention. Currently, pCTs have become the standard of care for RT treatment. However, all information yielding to sufficient tumor localization may be obtained equally from a dCT image.

Omitting pCT from the RT treatment pathway has drawn interest in the past few years, as there are several studies around the same topic with a varying approach [5–8]. Our specific intention was to evaluate if dosimetrically BMs could be treated with no pCT with equal accuracy, and without trying to replicate the original position. In addition, we tried to introduce which BMs would be able to be treated this way. The aim of the study was therefore to investigate the potential of using a dCT

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in palliative RT.

2. Materials and methods

2.1. Patient selection

This retrospective study was approved by the ethical committee of the Comprehensive Cancer Center of the Helsinki University Hospital. Altogether 60 BMs from 43 patients were treated with palliative RT. The average age of the patients was 70 years (range 36–92 years). BMs were located in eight bone sites (cervical, thoracic, lumbar, sacral vertebrae, iliac bone, acetabulum, costa, and long bones).

2.2. Data analysis

Data of dCT and pCT imaging, RT planning and the actual RT treatment cone beam computed tomography (CBCT) was used in analysis. The inclusion criteria contained documentation of BM treatment with palliative intent and a known diagnosis of cancer, acquired dCT with sufficient field of view (FOV) at a maximum of 30 days prior to pCT, and CBCT imaging for patient positioning before treatment. Mean time delay between dCT and pCT was 13 days (range 1–29 days).

Analyzed targets of palliative patients were obtained from oncologists' patient lists starting from March 2020 and targets were collected to get at least 5 targets per site (Table 1). Exclusion criteria for patients were fracture or fixed fracture between dCT and pCT, patient's arms or legs were lifted in either one of the CTs or patient had prosthesis in the treatment area.

dCT images were acquired from multiple manufacturers' CT scanners. Therefore, image reconstruction algorithms, FOVs, used tube currents and voltages varied between patients. These imaging parameter changes influenced dose calculations in RT plans, due to changes in Hounsfield units (HU). IAEA published thresholds +- 20 for HU difference used in RT [9], and Davis et al. [10] showed that 50 HU difference resulted 1% or less dose change in the treatment planning system (TPS) dose calculation. While tube voltage varied from 100 kV to 140 kV in dCT images, the treatment plan used the same HU calibration curve for 120 kV as used in pCT for mimicking the actual treatment protocol. In addition, we investigated the effect to the dose that occurred when 120 kV HU calibration curve was used instead of the 100 or 140 kV calibration curve.

Table 1
Anatomical sites, quantity of analyzed patients (n), planning technique, optimization, and dose volume histogram (DVH) criteria's of treatment plan for clinical target volumes (CTV).

CTV site	n	Planning technique	Optimization criteria	DVH comparing criteria
C-vertebra	9	posterior 5 field IMRT or VMAT of 2 half rotation	Normal tissue objective (priority 100, distance from target border 0.5 cm	$\lvert D(CTV_{V50\%})_{dCT}$-$D(CTV_{V50\%})_{pCT} \rvert$ $\lvert D(CTV_{V95\%})_{dCT}$-$D(CTV_{V95\%})_{pCT} \rvert$ right lung, mean dose left lung, mean dose right kidney, mean dose left kidney, mean dose heart, mean dose
Th-vertebra	13	posterior 5 field IMRT	Start dose 95% End Dose 10%, Fall-off 0.03), CTV + 6 mm (low-10% high + 10%, priority 100; low and high 50%=treatment dose, priority 80), health tissue (appropriate mean dose criteria, priority 80)	
L-vertebra	11	posterior 5 field IMRT or VMAT of 2 half rotation		
sacrum	6	VMAT of 2 half rotation		
ilium	5	VMAT of 2 half rotation		
acetabulum	5	VMAT of 2 half rotation		
costa	6	VMAT of 2 half rotation		
long bone	5	posterior 5 field IMRT or VMAT of 2 half rotation		
Total	60			

dCT images with the planned treatment area, were imported and fused using rigid translation and rotation movements to pCT images employing treatment planning software (Eclipse, 16.1.10, Varian Medical System Inc., Palo Alto, USA). The entire affected bone compartment was contoured in the clinical target volume (CTV). An arbitrary 6 mm margin was added around CTVs to create planning target volumes (PTVs). Organs at risk (OARs) in the close proximity (<5 cm) of the treatment area were contoured to both dCT and pCT images if the whole organ was visible.

Although patients' positioning changed from curved couch in dCT to flat couch in pCT and the actual RT treatment, straight couch contour was added to both image sets, for avoiding dose change due to couch absorption in dose calculation [11].

The chosen RT planning technique was similar to the standard RT treatment used in Helsinki Cancer Center for palliative BM RT. We used intensity-modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) techniques in RT planning with Acuros dose calculation algorithm (Acuros External Beam, version 16.1.0, Varian Medical System Inc., Palo Alto, USA) for achieving more conformal dose distributions with better target volume coverage and sparing of healthy tissues compared to conventional radiotherapy techniques [12]. As they require more accuracy from patient settings and planning imaging and are slower to treat with standard C-arm gantry, they are not so widely used for palliative patients. However, a novel ring style gantry Halcyon 2.0 (Varian Medical System Inc., Palo Alto, USA), with flattering filter free (FFF) mode beam and fast gantry and collimator rotation [13] makes IMRT and VMAT treatments faster than a standard linear accelerator and was therefore used in this study.

The treatment dose was normalized using ICRU criteria (ICRU Report 95) to cover 50% of PTV ($D_{V50\ \%} = 100\%$). The planning technique and optimization criteria used in this study are shown in Table 1.

Treatment plans were copied to fused pCT images with fixed monitor units for investigating all the differences that could affect the delivered dose, i.e. couch shape, HU variations, patient positioning, target growth and dose calculation.

Dose volume histograms (DVH) of treatment plans made for dCT and transferred to pCT images were compared, and the differences in CTVs' dose in 50% volume, $D(CTV_{V50\%})$, and 95% volume, $D(CTV_{V95\%})$, were calculated. Mean doses of healthy tissues were compared.

2.3. Treatment

Patients were treated with several different palliative fractionation doses, ranging from 1 × 8 Gy (13 patients) to 5 × 4 Gy (44 patients) and 10 × 3 Gy (3 patients). For patient positioning, CBCT images were taken in every fraction and matched with translation direction to dCT images without rotation correction to mimic the couch movement of Halcyon. The match was considered acceptable, if the treated target area fit to the CTV in the dCT image within a 6 mm margin (our chosen PTV). The match was considered not acceptable if in any of the fractions CTV failed to fit into the margin.

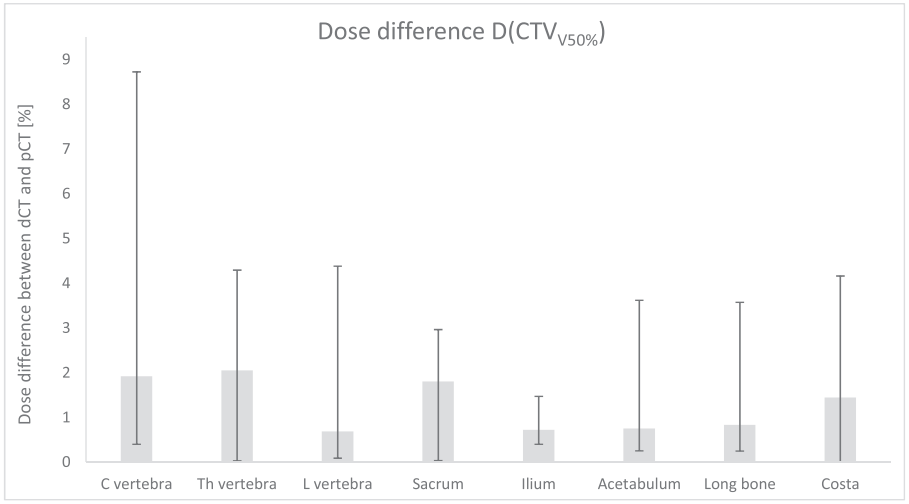
2.4. Statistics

Wilcoxon signed rank test was used to test significances. Test was performed with a significance level of $p < 0.05$.

3. Results

The dose differences between dCT and pCT plans in 50%, $D(CTV_{V50\%})$, and 95%, $D(CTV_{V95\%})$, volume of CTV are shown in Fig. 1. The range of dose differences in the cervical vertebra stands out in both $D(CTV_{V50\%})$ and $D(CTV_{V95\%})$, which medians and ranges were 1.9 % (0.4–8.7%) [p = 0.31] and 3.7 % (0.5–9.5%) [p = 0.09], but these

a)



b)

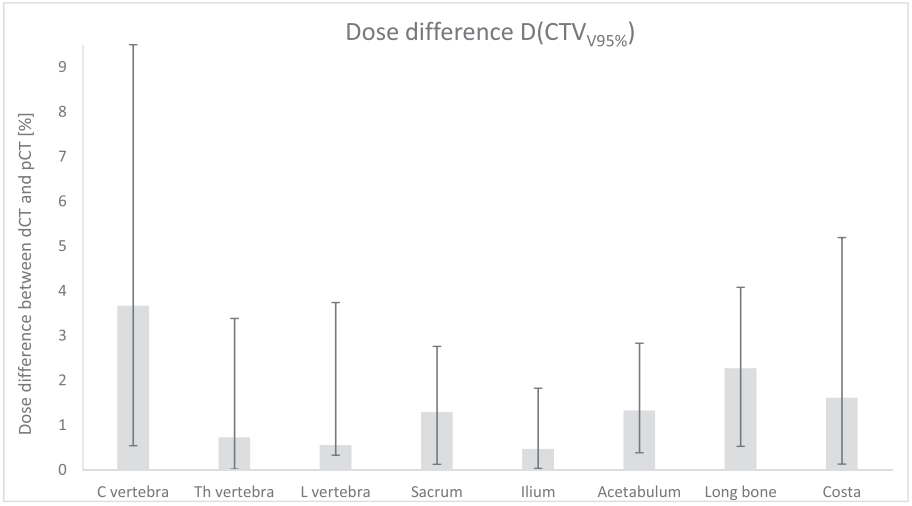


Fig. 1. Median dose difference with ranges between plans calculated for diagnostic CT (dCT) images and planning CT (pCT) images shown as a) 50% and b) 95% volume of CTV.

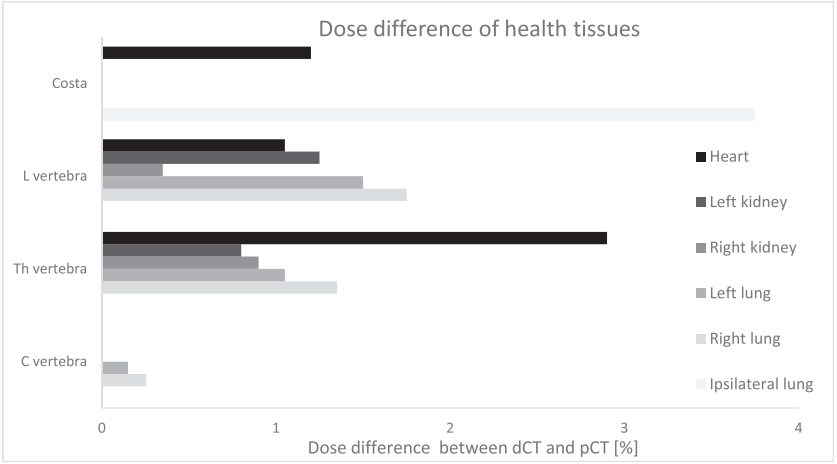


Fig. 2. Median dose difference between plans of diagnostic CT images and planning CT images shown in mean volume of healthy tissue.

differences were not significant. Long bones showed significant 2.3 % (0.5–4.1%) [p = 0.04] difference in D($CTV_{V95\%}$), however in D($CTV_{V50\%}$) the dose difference remained at 0.8 % (0.3–3.6%) [p = 0.04] but was significant. Also thoracic vertebra in D($CTV_{V50\%}$) with difference of 2.1 % (0.0–4.3%) [p = 0.01] and acetabulum in D($CTV_{V95\%}$) with difference of 1.3 % (0.4–2.8%) [p = 0.04] were significant. Median dose difference of all the other sites stayed under 2% (0.0–5.2%), and none of these changes were significant.

Differences in mean OAR doses in pCT and dCT plans are shown in Fig. 2. The median change in OAR was 1.3% (range 0–6.7%). Highest median dose difference was in ipsilateral lung in costa treatments 3.8% (0.3–4.7%). In symmetrical treatments regarding vertebra, the median difference of mean heart dose was 2.0% (0.1–6.7%), left and right lung 1.2% (0.0–4.7%), and left and right kidney 0.9% (0.1–5.0%). None of these differences were significant.

The maximum effect to the dose between the 120 kV and 100/140 kV HU calibration curve was 1.4% (Table 2).

Match of CTV with added 6 mm margin in dCT images and treated CBCT images was found to be 100% acceptable for every other site except for thoracic vertebra (92%), cervical vertebra (78%), costa (67%) and only 50% for long bone.

4. Discussion

Our study showed that, based on the small but representative sample of various sites, BMs located in the thoracic, lumbar, and sacral spine and pelvis could be accurately and safely treated based on a dCT image only.

To omit pCT from the RT treatment planning – and to use the existing dCT instead - is a novel approach. However, in the latest years a few similar studies have been made coming to the same conclusion. A study by Wong et al. reviewed 150 dCT scans comparing them to pCTs to review potential barriers to radiation planning, but finally only a subset of 33 patient data sets was used to assess HU variance and dosimetric impact. The 95% dose coverage of the PTV between the dCT and the CBCT-modified-dCT varied between −2% and +2.5% [5]. They subsequently treated 30 patients with a RT treatment plan done on the dCT, by using a full-body vacuum bag to replicate the curvature of a dCT. Wong's work was followed by its implementation experience by Schuler et al. treating 160 patients with BM or soft-tissue metastases without pCT, with replicating the dCT position of patient set-up for treatment. The primary endpoint in Schuler's study was the proportion of palliative patients eligible for the CT simulation-free pathway [6], so it did not assess the treatment accuracy of the dCT used in the planning.

Glober et al. studied retrospectively the applicability of dCT for RT treatment, focusing on critically ill patients in intensive care unit. They treated 10 patients based on dCT using simple parallel-opposed fields. The study revealed excellent target coverage and acceptable hot spots, and the department has adopted this approach for critically ill patients [7]. In addition, Ho et al. reviewed 10 patients and compared the treatment plans concentrating on the change in tumor volume, with soft-tissue metastases being included [8].

Comparing our study to the two most extensive studies by Wong and Schuler, they differed in several ways from ours. We used more specific target volumes, i.e. CTVs instead of PTVs, and CTVs were contoured by a radiation oncologist both on the dCT and on the pCT, separately. This enabled an accurate interpretation between the two RT treatment plans. Also, they tried to replicate the original position of the dCT by using a curved full-body vacuum bag in the treatment process. However, as the main objective of implementing the use of dCT is rather to simplify and hasten the RT process in a palliative setting, we do not approve the idea of trying to achieve the original position of the dCT with supplementary effort.

All the works above also contained soft-tissue metastases rendering the data more heterogenous. The authors in the other studies did not specify which locations of metastases would fit into their treatment pathway. We are presenting in our study BMs in all most common different locations including ribs and extremities (femur, humerus) and cervical spine.

Our findings were very much in line with those from the other studies, indicating that dCT in RT planning is highly usable. However when applied to clinical setting there are issues that need yet to be assessed.

Not all BM patients can be treated without a pCT. Patients may be referred to a palliative RT with no dCT, but with an MRI or an X-ray image or in some cases the referrals are only symptom-based. There may be anatomic changes and thus CBCT-images should be carefully reviewed. The patient position in the dCT should be reproducible in the treatment set-up.

In our study, the diagnostic images were on average 13 days old. In the study by Ho et al., the researchers reported the median daily growth of the metastasis being 1.8%, however they included soft-tissue metastases in their study and especially lung metastases were observed to grow rapidly. We do not consider the speed of growth very relevant to our study, as we treat the entire affected bone compartments.

CTVs of BMs may be created either by isotropic expansion of the GTV or by delineation of the affected bone compartment [14]. In this study, the affected bone compartment was used. We used a 6 mm margin for PTV. Little consensus exists for suggested margins from CTV to PTV in palliative BM RT treatment [14]. Margin of 6 mm was chosen to mimic the standard clinical practice, by using even stricter PTV margins (often a 7–10 mm margin is used in BM RT treatment based on clinical practice).

The error generated from patient positioning, couch shape, and dose calculation was in most our cases lower than 2%. This is considered an acceptable error, as in a RT process acceptance levels of accuracy in the dose delivered to the dose specification point varies from 3.5% to 5% [15]. CTV dose difference between pCT and dCT was up to 3% for upper

Table 2
The absolute dose difference on diagnostic CT images taken at 100 or 140 kV, when the 120 kV electron density calibration curve is used instead of the 100 or 140 kV calibration curve.

	Technique	$\Delta D(V_{95\%})_{CTV}$, {%}		$\Delta D(V_{50\%})_{CTV}$, {%}		$\Delta D(V_{50\%})_{Spinal\ Canal}$, {%}	
		Average ± SD	Maximum	Average ± SD	Maximum	Average ± SD	Maximum
C vertebra (n = 7)	IMRT + VMAT	0.4 ± 0.3	0.9	0.3 ± 0.2	0.8	0.3 ± 0.3	0.8
Th vertebra (n = 8)	IMRT	0.3 ± 0.2	0.5	0.2 ± 0.2	0.5	0.3 ± 0.2	0.6
L vertebra (n = 8)	IMRT + VMAT	0.6 ± 0.4	1.4	0.4 ± 0.2	0.8	0.4 ± 0.2	0.7
All areas (n = 22)	IMRT	0.4 ± 0.4	1.4	0.4 ± 0.2	0.8	–	–
All areas (n = 13)	VMAT	0.2 ± 0.1	0.3	0.1 ± 0.1	0.2	–	–

The notation $D(V_X)_{CTV} = Y\%$ means that the dose Y% will be in the volume fraction of the CTV X%.

vertebra and long bones, but stayed low for thoracic, lumbar and pelvic area.

Fitting CTV into CBCT images in patient set-up was based on the results of CTV dose changes. CTVs of cervical vertebra, costa and long bone failed to fit into 6 mm margin in more than one patient, whereas CTVs of lumbar vertebra, sacrum and pelvis fully succeeded and only one of 13 thoracic vertebra patient's set-up was not acceptable.

Results of OAR dose showed one of the limitations of this method. Differences in ventilation phase between dCT and pCT may result in dose escalation in heart when treating thoracic vertebra and ipsilateral lung in costa treatment. Free ventilation was used in pCT images but ventilation in dCT was unknown. Mean dose of kidneys and lungs remained below 1.8% in other sites.

In our simulations variation of dose, recruiting 120 kV electron density calibration curve to images taking with 100 kV or 140 kV, was up to 1.4%. Davis et al. showed that 50 HU difference resulted in 1% or less dose change in TPS calculation [6]. Variation of HU value to dose calculation is significantly smaller than e.g. dose prediction accuracy of Acuros dose calculation algorithm used in this study. Rana et al. showed that the dose errors of Acuros XB algorithm prediction is up to 3.8% for different field sizes and air gap thickness [16]. We discovered that dose changes in patients with prosthesis are greater but excluded the results due to small number of patients.

We propose specific criteria for the use of dCT in RT treatment planning. The patient should have a dCT of decent quality and with FOV available, also the diagnostic image should not be older than a month. The location of the BM should be one of the following: thoracic, lumbar, sacral vertebrae or pelvis. The patient should have no external immobilization devices (i.e. positioning of the patient should be fully reproducible) and with no prothesis in the treatment area. There should not have happened any anatomic changes (e.g. fractures, suspected enlargement of the metastasis) in between the time of dCT and the RT treatment, emphasizing on the importance of the anamnesis and clinical examination.

We hypothesize that a larger volume of the target may affect the treatment possibility based on dCT, but this was not investigated further. Caution must be exercised with CTVs encompassing large anatomic areas, as the patient positioning in the dCT may be challenging to reproduce.

When taken into clinical practice, we must carefully evaluate the criteria presented above, and to assess the numbers of BM patients fitting into these criteria. Schuler et al. approximated that around third of the patients were eligible to be successfully treated with the pCT-free treatment path [11], however at the end of their study the proportion increased to half of the patients, when access to systems of external radiology providers to download dCT scans was improved and the protocol extended to include IMRT.

One may argue why we used IMRT/VMAT techniques in our study, as when treating frail palliative patients sparing healthy tissue and avoiding late toxicities should not compromise the ideal of a fast and simple treatment path. However, with Halcyon, or similar compact ring style treatment systems becoming standard devices, treating with intensity modulated plans do not take longer [17]. Radiation therapy treatments planned in this study could be also translated to all linear accelerators that are capable of treating IMRT/VMAT techniques. Our study shows that using dCTs instead of a pCT is feasible even with more complex RT techniques (IMRT/VMAT). There is no evidence yet that any technique is superior when delivering palliative radiation doses [14].

The limitation of the study was its small size and retrospective approach. When the use of dCT in RT treatment planning will be taken into clinical practice, careful thought and further investigation will be needed, on how the clinical flow will benefit from this. Our intention is also to review in the future the potential of treating soft-tissue metastases based on dCTs.

In conclusion, this study showed the potential of using dCT images in palliative RT planning of BMs in thoracic, and lumbar spine and pelvic sites. This dCT based planning strategy will be applied clinically for these BM sites.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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